

Long-term results after treatment of basal cell carcinoma of the eyelid in Southwestern Finland

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PURPOSE. Basal cell carcinoma (BCC) is the most common skin cancer of the eyelid, showing an increasing incidence in the white population. The authors studied the clinical characteristics and the treatment results of BCC of the eyelid in southwestern Finland during 1977-1997.

METHODS. The authors reviewed the case records of 191 patients with BCC of the eyelids treated at the Turku University Eye Clinic during 1977-1997. The mean follow-up period after the treatment was 8.6±5.2 years.

RESULTS. The 191 patients had altogether 194 BCC tumors of the eyelid with the mean diameter of the tumor being smaller than 10 mm in 77.3% of cases. Of the 194 BCC tumors of the eyelid 16.0% showed recurrence, and the recurrence rate of all surgically treated tumors was 13.7%. In this study 61 patients (31.9%) developed other malignancies than the BCC of the eyelid including 28 patients (14.7 %) with carcinoma in other locations than skin.

CONCLUSIONS. Incompletely removed BCCs of the eyelid showed only 18.9% recurrence rate during the follow-up time. On the other hand, BCCs of the eyelid should not be underestimated because of the rather high total recurrence rate. The frequency of 31.9% of other malignancies than BCC of the eyelid is remarkably high and requires special attention from the ophthalmologist taking care of the patient with BCC of the eyelid. (*Eur J Ophthalmol* 2007; 17: 494-500)

KEY WORDS. Basal cell carcinoma, Eyelid, Follow-up, Localization, Recurrence, Treatment

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INTRODUCTION

Basal cell carcinoma (BCC) is the most common skin cancer of the eyelid, accounting for 80-90% of cases (1). Its incidence more than tripled in southwestern Finland from 1977 through 1997, showing a rise with age (2). The most common treatment methods of BCC of the eyelid include surgical excision, cryotherapy, radiotherapy, and laser surgery (3). There are only a few earlier studies on the clinical characteristics of BCC of the eyelid from Scandinavia (4, 5). We studied clinical characteristics and treatment results of BCC of the eyelid in southwestern Finland from 1977 through 1997, with special reference to the frequency of recurrences of BCC of the eyelid removed by

using a traditional excision, and the occurrence of other malignant diseases in patients with BCC of the eyelid.

METHODS

The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki, as renewed in 2000. The study protocol was approved by the Ethics Committee of the University of Turku and the Turku University Central Hospital.

We studied the clinical characteristics and the treatment results of BCC of the eyelid in the region of southwestern Finland during the years 1977 through 1997. During these

Fig. 1 - Distribution of 194 cases of basal cell carcinoma (106 cases in the right eye and 88 cases in the left) into different areas of the eyelid.

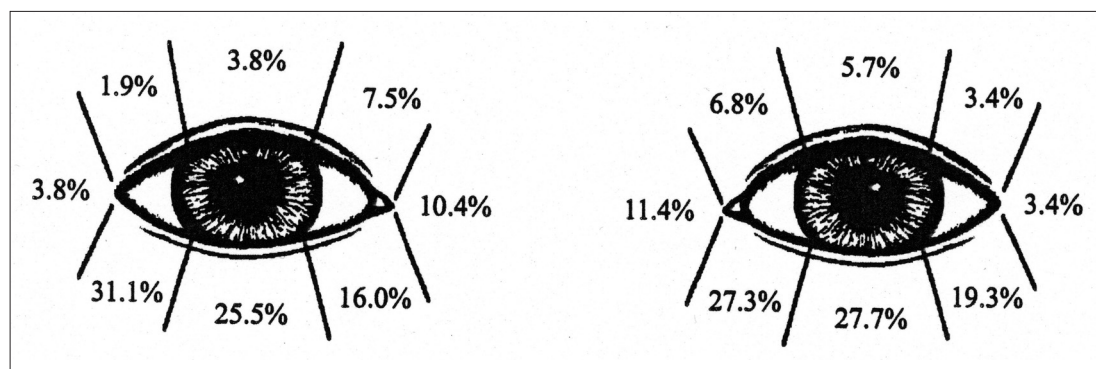


TABLE I - DISTRIBUTION OF NUMBER, AGE, SEX, AND POSTOPERATIVE FOLLOW-UP OF PATIENTS WITH BASAL CELL CARCINOMA OF EYELID

	No.	Age (years), mean \pm SD	Follow-up (years), mean \pm SD
Men	94	68.4 \pm 12.2	8.1 \pm 5.1
Women	97	70.1 \pm 12.0	9.1 \pm 5.2
Total	191	69.3 \pm 12.0	8.6 \pm 5.2

years practically all malignant tumors of the eyelid in the region of southwestern Finland were treated at the Turku University Eye Clinic and the hospital record analysis alone provided a nearly complete collection of symptomatic BCC cases in this area. We reviewed the case records of BCC of the eyelid treated at the Turku University Eye Clinic during the years 1977 through 1997. Eyelid tumors seen both in the outpatient and inpatient clinics were included.

There were altogether 194 BCC tumors in 191 patients, including 94 men and 97 women, with a mean age of 68.4 \pm 12.2 (range 35 to 88) years in men, 70.1 \pm 12.0 (range 31 to 89) years in women, and 69.3 \pm 12.0 (range 31 to 89) years in all patients (Tab. I).

Tumor location was classified as upper and lower lid; medial, middle, and temporal thirds; and medial and lateral canthal region (Fig. 1). The anatomic location of the tumors of the eyelid was classified as margin of the eyelid, pretarsal part, preseptal part, canthal region, and diffuse, including those cases which were more widespread and located in several of these areas. Pretarsal area of the eyelid was used to describe the area of skin in eyelids from eyelashes 4 mm downwards in lower lid and from eyelashes 10 mm upwards in upper lid. Preseptal area of the eyelid was used to describe the area of skin from 4

mm below eyelashes to bony orbital margin in lower lid and from 10 mm higher than eyelashes to eyebrows in upper lid. Tumors were distributed according to macroscopically measured tumor size into groups of 1-4 mm, 5-9 mm, 10-14 mm, 15-19 mm, and 20 mm or larger.

Excisional biopsy was taken from 83 tumors before operation and histopathologic confirmation was done in all surgically operated tumors. Those tumors, which were treated either with radiation therapy or cryotherapy, were all confirmed as BCC by excisional biopsy. All specimens were submitted for paraffin sections. From histopathologic sections, excisions were classified as radical when there were about one fourth of the tumor diameter size healthy tissue margins seen in histologic sections. In marginal excision there needed to be a certain measurable (at least 0.1 mm) healthy tissue margin seen in histologic sections. In intralesional excision there were no measurable healthy tissue margins seen in histologic sections.

Surgical operation was performed altogether in 175 tumors. The tumor was excised with a 2-4 mm margin of normal looking tissue. Radiation therapy was used in 13 cases and cryotherapy in 3 cases as primary therapy. Routinely, macroscopic clinical examination was carried out 1 month after the operation at University Eye Clinic, and after that control examinations were carried out in private offices. All cases showing a recurrent BCC of the eyelid after the treatment returned to the University Eye Clinic for new management. The mean follow-up period after the treatment was 8.1 \pm 5.1 years in men, 9.1 \pm 5.2 years in women, and 8.6 \pm 5.2 years overall (Tab. I).

Descriptive statistics, i.e., percentages and 95% confidence intervals (95% CI), and statistical analyses were performed using SAS for Windows version 8.2. The tests for association between categorical variables eye (right/left) and location of BCC in eyelid (3 categories) were performed using Pearson chi-square test. The sta-

tistical test was two-sided and was performed using a 5% significance level. The results are expressed as mean \pm SD.

RESULTS

The distribution of the location of the 194 BCC tumors is shown in Figure 1. There were no statistically significant differences in the distribution of the location of BCC of the eyelid between the right and left eyes (Pearson chi-square 5.5776, $p=0.06$). The anatomic location of the 194 BCC tumors was available in 192 cases. It comprised the margin of the eyelid in 96 cases of which 19 showed recurrence (19.8%), the pretarsal area in 56 cases of which 4 recurred (7.1%), the preseptal area in 31 cases of which 7 recurred (22.6%), diffuse extension in 2 tumors with no recurrence, and the canthal region in 7 cases of which 1 (14.3%) showed recurrence (Tab. II). During the first period of the study (1977-1986) there were 12 recurrences (16.7%) and during the second period of the study (1987-1997) there were 19 recurrences (15.6%).

Information on tumor size was available in 176 cases. The size of the tumor at diagnosis is shown in Table III. In

about one half of the cases with BCC of the eyelid the mean diameter of the tumor was between 5 mm and 9 mm. When the first and second periods of the study were compared, the groups of the large tumors (15 mm or more) showed somewhat higher proportion in the second period of the study (Tab. III).

Surgical operation was performed in 175 cases. Local anesthesia was used in 152 cases and general anesthesia in 23 cases. In 16 cases various local flaps were used depending on the tumor size, location, and depth. In 7 cases skin transplants were used to achieve wound closure. In 11 cases tissue transplants and various local flaps were combined in the wound closure. In 13 patients primary treatment was radiation therapy and in 3 patients cryotherapy. The surgical operation was done by ophthalmologists in 131 cases, plastic surgeons in 40 cases, and otolaryngologists in 4 cases.

Of the 194 BCC tumors of the eyelid, 31 (16.0%) showed recurrence. The recurrence rate of all surgically treated tumors was 13.7% (Tab. IV). Almost all recurrent tumors were seen in the group of excision and only one case recurred in the group of skin transplant. In the group of radiation therapy the recurrence rate was 46.2% and in the group of cryotherapy it was 33.3%. In the treatment of the

TABLE II - ANATOMIC LOCATION OF BASAL CELL CARCINOMA IN EYELID

	Right eye, n	Left eye, n	Total, n	Recurrence rate of BCC %	95% CI
Margin of eyelid	54	42	96	19	19.8 12.4-29.2
Pretarsal	27	29	56	4	7.1 2.0-17.3
Preseptal	19	12	31	7	22.6 9.6-41.1
Diffuse	1	1	2	0	
Canthal region	4	3	7	1	14.3 0.4-57.9

TABLE III - CALCULATED MEAN DIAMETER OF BASAL CELL CARCINOMA OF THE EYELID

Diameter, mm	1977-1997, frequency (%)	1977-1986, frequency (%)	1987-1997, frequency (%)
1-4	47 (26.7)	22 (32.4)	25 (23.1)
5-9	89 (50.6)	34 (50.0)	55 (50.9)
10-14	22 (12.5)	9 (13.2)	13 (12.0)
15-19	10 (5.7)	1 (1.5)	9 (8.3)
20 or over	8 (4.5)	2 (2.9)	6 (5.6)
Total	176 (100)	68 (100)	108 (100)

31 recurrent tumors altogether 54 new treatment procedures were done (Tab. IV).

Histopathologic examinations showed that 80 (45.7%) of the surgically treated tumors were radically removed, 36 (20.6%) were marginally removed, and 59 (33.7%) had intralesional margins. Recurrences were seen after radical excision in 6 cases (7.5%), after marginal excision in 3 cases (8.3%), and after excision with intralesional margins in 15 cases (25.4%) (Tab. V).

Postoperatively 14 cases developed lacrimal stenosis, which occurred in 8 cases in the lower canaliculus, in 2 cases in the upper canaliculus, and in 4 cases in both canaliculi. Postoperative changes of the lid included entropion in 4 cases, ectropion in 14 cases, lagophthalmus in 3 cases, and trichiasis in 4 cases. Postoperative plastic reconstructive surgery was needed in 10 cases.

Altogether 61 patients with BCC of the eyelid had concomitant malignant disease in other location. The distribution of malignant diseases in the patients with BCC of the eyelid is shown in Table VI. There were altogether 61 patients who had malignant diseases other than BCC of the

eyelid. BCC in other location than the eyelid was found in 29 patients, and together with another malignancy in 7 patients. There were 17 patients with carcinoma, 2 patients with myeloma, and 1 patient with lymphoma.

DISCUSSION

In this study we used the traditional excision technique (6) with the principal aim of complete eradication of the tumor, preservation of normal tissue as much as possible, and good reconstructive result with minimal subsequent interventions. This traditional technique is less expensive and less time consuming than the Mohs technique, which is well-suited for eyelid BCC with ill-defined borders or recurrent tumors (5) or due to its low recurrence rate for high-risk cases of periocular BCC (7). The recurrence rate of surgically treated BCC of the eyelid in this study was 13.7%, which is higher than the recurrence rate of 0-7.8% after removing BCC of the eyelid by using the Mohs micrographic technique (7, 8). However, in an earlier study

TABLE IV - TREATMENT OF BASAL CELL CARCINOMA (BCC) OF THE EYELID

Method of treatment	Number of tumors	Recurrent BCC			
		No	%	(95% CI)	Retreatment
Operation	175	24	13.7	(9.0-19.7)	36
Excision	141	23	16.3	(10.6-23.5)	36
Flap	16				
Graft	7	1	14.3	(3.6-57.9)	*
Flap with graft	11				
Radiation therapy	13	6	46.2	(19.2-74.9)	8
Cryo therapy	3	1	33.3	(0.8-90.6)	10

* No retreatment because of poor general condition

TABLE V - RECURRENT BASAL CELL CARCINOMA OF EYELID FOLLOWING SURGERY AND DIFFERENT POSTOPERATIVE TREATMENT METHODS

Surgery	No.	Retreatment due to partial excision			Recurrent		
		Surgery	Radiation therapy	Cryotherapy	Number	%	95% CI
Radical	80				6	7.5	2.8-15.6
Marginal	36	1			3	8.3	1.8-22.5
Intralesional	59	10	8	1	15	25.4	(15.0-38.4)
Total	175	11	8	1	24	13.7	9.0-19.7

TABLE VI - DISTRIBUTION OF MALIGNANT DISEASES IN PATIENTS WITH BCC OF EYELID

Malignancy	Men	Women	Total
BCC in other location	16	13	29
SCC	1	1	2
Carcinoma	8	9	17
Breast		5	5
Prostate	3		3
Urinary tract	1	1	2
Esophageal		1	1
Pulmonary	1	1	2
Pancreatic	1		1
Rectum	1		1
Kidney	1		1
Colon		1	1
Myeloma	2		2
Lymphoma	1		1
BCC + carcinoma	5		5
BCC + SCC		1	1
BCC + melanoma	1		1
SCC + carcinoma	1		1
Other	1	1	2
Total	36	25	61

BCC = Basal cell carcinoma; SCC = Squamous cell carcinoma

the recurrence rate of 23% has been reported when traditional excision technique was used without microscopic monitoring during the surgery (1). In a recent study Mohs micrographic technique was compared with the traditional excision technique, and it was observed that although the recurrence rates were lower after Mohs technique than after surgical excision, the differences were not significant (9).

In our material radically excised tumors showed 7.5% recurrence rate. This may be explained by the fact that the normal histologic sections cover only a small part of the tissue margin. Routine bread loaf sections of a tissue block are taken at no closer than 2 mm intervals, providing direct examination of less than 1% of the tissue margin (10). On the other hand, even with Mohs micrographic surgery technique with all microscopically controlled free margins of the tumor, the recurrence rates are presented to be between 0.0% and 7.8% for primary and recurrent tumors during 5 years follow-up (7). It has been reported that recurrence after apparent complete excision could arise from discontinuous tumor, or alternatively, new tumor at or beyond the edge of scar could be a further primary unconnected tumor with the original lesion (11).

However, from 95 incompletely excised tumors, 18 recurred (recurrence rate 18.9%). This is lower than mentioned in the literature (1, 4). It has been published in recent studies that regardless of treatment modality, BCCs have been described not only to spontaneously progress but also to regress (12, 13). Walker and Hill showed that recurrence rate after excision of a primary BCC with histologic margin involvement gave total recurrence rate of 38% during 5 years follow-up based on 12 referred articles (10).

Low recurrence rates have been achieved with some limitations also after cryotherapy (14-16). In this study cryotherapy was used only for a short period of time (from 1988 through 1990). In one of our cases the aim of cryotherapy was to shrink the tumor size before operation.

In our study, high recurrence rate in patients treated with radiation therapy may be due to patient selection. In this study radiation therapy was used for the oldest patients who could not be operated.

In some cases radiation therapy is most beneficial for patients who cannot tolerate surgical excision or who decline surgical therapy (3).

There were no statistically significant differences between both eyes in the location of BCC of the eyelid. A majority of tumors were situated on the lower eyelids, which is in a good agreement with previous reports (17-19). However, in our study only 11% of tumors were situated on nasal canthal area, which is much less than shown in previous reports (20-25%) (17-19).

In this study, 61 patients (31.9%) developed other malignancies than the BCC of the eyelid. In earlier studies it has been shown that patients with BCC of the skin have a higher risk to develop a new skin cancer or a variety of cancers following an initial diagnosis of BCC (20). In this study in the 191 patients with BCC of the eyelid the calculated annual prevalence of all 61 non-eyelid malignancies was 1520/100,000 which is 3.8 times higher than the annual incidence of 400/100,000 observed in working-aged Finns during the years from 1971 through 1985 (21). The increase in the risk for subsequent cancer could be partly explained by the increased clinical alertness devoted to patients treated for skin cancer (22). Other explanations may be ultraviolet (UV)-induced immunosuppression (23-25), some common carcinogenic (viral?) agent, or both together.

Practicing ophthalmologists should pay attention to BCC and other malignant changes of the eyelids. Aging of the

population and larger amount of UV B radiation reaching the surface of the earth as a result of ozone depletion in the atmosphere may contribute to increase in the incidence of these diseases (26). It has been estimated that if no control measures are enforced, 223 annual additional cases of skin cancer per million at risk will occur by the year 2030, and 1890 cases per million by the year 2070 in the United States (27).

In summary, incompletely removed BCCs of the eyelid showed only 18.9% recurrence rate during follow-up. However, these tumors should not be underestimated because of the rather high total recurrence rate. In addition, nearly every third of these patients had another malignancy.

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